New Bowel Preparations for Colonoscopy

a report by

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Despite advances in endoscopic imaging such as high-definition technology, wide-angle objectives and narrow-band imaging, the ability to visualise abnormalities on the bowel wall may be limited by the quality of bowel preparation. Approximately 25% of bowel preparations performed for colonoscopy are inadequate,\(^1,2\) which results in a reduction in the detection of colorectal neoplasms, a prolonging of procedure times, a decrease in caecal intubation rates and an increase in the total number of colonoscopies and the costs of colorectal cancer screening. Recently, new bowel cleansing regimens have been introduced that are highly effective, safe and well tolerated by patients. Improvements in bowel preparation for colonoscopy will improve patient compliance with colorectal cancer screening guidelines and the efficiency and outcome of colonoscopy.

The Role of Bowel Preparation in the Outcome of Screening Colonoscopy

The quality of bowel cleansing can significantly influence the detection of adenomas and colon cancer. In a retrospective analysis of over 5,000 colonoscopies, Leaper reported 17 missed colon cancers, with poor visualisation of adenomas and colon cancer. In a retrospective analysis of over 5,000 colonoscopies and the costs of colorectal cancer screening. Recently, new bowel cleansing regimens have been introduced that are highly effective, safe and well tolerated by patients. Improvements in bowel preparation for colonoscopy will improve patient compliance with colorectal cancer screening guidelines and the efficiency and outcome of colonoscopy.

Efficiency and Cost of Colonoscopy

Poor bowel preparation can influence the efficiency and cost of colonoscopy. Studies have shown that inadequate bowel preparation has been a significant predictor of prolonged caecal intubation time (>20 minutes; p=0.0077),\(^3\) prolonged (>10 minutes) insertion time (odds ratio [OR] 2.80, 95% confidence interval [CI] 1.41–5.56; p=0.003)\(^4\) and lower caecal intubation rate (90 versus 71%; p<0.007).\(^5\) These measures of tolerability include the adverse event profile of the product and the patient compliance rate. Common adverse events associated with colonoscopy include abdominal fullness and pain, nausea, vomiting, dizziness and bloating.\(^6,7\) Caution should be exercised when using PEG-based preparation products in patients with oesophageal obstruction or known hypoaesthesia, and those at increased risk of electrolyte abnormalities (thiazide diuretics).

Patient Safety

The colon cleansing agents have an excellent safety profile, considering that more 15 million doses are administered annually in the US. Nonetheless, adverse events have been rarely reported with all bowel preparations. Between 1997 and 2002, the US Food and Drug Administration (FDA) received 34 and 100 reports of serious adverse events related to the use of sodium phosphate (NaP) and polyethylene glycol (PEG), respectively.\(^8,9\) The most serious adverse event associated with NaP is nephrocalcinosis, usually in patients with pre-existing renal insufficiency. Markowitz recently described 21 cases of renal failure and nephrocalcinosis temporally related to the use of NaP. The risk of acute phosphate nephropathy can be minimised by careful attention to patient selection and emphasising the importance of adequate hydration before, during and after colonoscopy.\(^10,11\) The use of PEG formulations has been associated with several adverse events, including seizures (usually associated with hyponaetria and hypokalaemia), Mallory-Weiss tears (related to retching and vomiting), hypothermia, cardiac arrhythmias and dysnatremia.\(^12,13\) Caution should be exercised when using PEG-based preparation products in patients with oesophageal obstruction or known hypoaesthesia, and those at increased risk of electrolyte abnormalities (thiazide diuretics).
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New Products and Revised Formulations

The three classes of bowel preparations are osmotic agents, PEG-based solutions and stimulants. Over the past few years many of the original bowel preparations have been modified or changed to make the preparation better tolerated by patients. Improvements include enhanced taste, a reduction in volume and fewer tablets. These advances are likely to improve patient compliance, resulting in a more effective bowel cleansing and, consequently, enhanced efficacy in colorectal cancer prevention.

Sodium Phosphate

Patients taking bowel preparations containing NaP need to consume appropriate amounts of fluid to avoid electrolyte imbalance and dehydration.11 NaP bowel preparations should not be used in patients with impaired renal function, congestive heart failure or hypercalcaemia. In addition, caution is recommended when administering to patients with a pre-existing electrolyte disturbance or to debilitated or elderly patients. Transient electrolyte abnormalities are common with NaP, but are rarely associated with serious adverse events.

OsmoPrep®

The original NaP tablet formulation dosing regimen (Visicol®, Salix Pharmaceuticals, Inc., Morrisville) consisted of 32–40 tablets: 20 tablets taken the evening before colonoscopy and 12–20 tablets taken three to five hours prior to the colonoscopy.19 Due to the presence of microcrystalline cellulose, an insoluble excipient that could potentially obscure visualisation of the colon, a new formulation was developed. The new NaP tablet formulation, OsmoPrep® (Salix Pharmaceuticals, Inc., Morrisville), consists of smaller and smoother tablets with a waxy surface associated with serious adverse events.

Newer reformulated bowel preparations appear to be better tolerated and easier to complete. Improved tolerability and compliance result in a more effective bowel cleansing and, consequently, enhanced efficacy in colorectal cancer prevention.

Polyethylene Glycol

There are various 4l and 2l PEG products available on the market in the US. Each differs with respect to volume, electrolyte content, requirement of adjunctive laxative and the presence of artificial sweeteners. The 2l PEG preparations were developed because many patients were unable to ingest the entire 4l PEG. Numerous adverse events such as bloating, abdominal fullness, nausea or vomiting. PEG products are safe in most patients, but there have been serious reports of seizure, hyponatremia, intestinal perforation, aspiration and Mallory-Weiss tears.3,12

MoviPrep®

MoviPrep® is the most recent 2l PEG product to be approved for bowel cleansing prior to colonoscopy in the US. MoviPrep contains PEG 3350, but also contains ascorbic acid, which acts as an osmotic agent, enhancing the bowel cleansing efficacy of the product. The recommended dose of MoviPrep is 2l (approximately 64oz) of solution.
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(with one additional litre of water) taken orally prior to the colonoscopy. Patients have the option to take the preparation the evening before the colonoscopy or as a split-dose, the first dose (11) the evening before colonoscopy and the second dose (10) at least one hour prior to colonoscopy.

In a study comparing MoviPrep and 4L PEG, acceptable colon cleansing was comparable in both treatment arms (88.9 and 94.8%; p = not significant [NS]) using a split-dosing regime.22 A significantly greater proportion of patients who received MoviPrep versus 4L PEG rated the degree of satisfaction, overall acceptability of gut cleansing regimen and taste of the preparation better for MoviPrep. In a study comparing MoviPrep with NaP solution administered as a single dose the evening prior to the examination, acceptable colon cleansing was similar in both treatment groups (72.5 versus 63.9%; p=NS).23 A significantly greater proportion of patients who took MoviPrep versus NaP solution reported the taste of the solution as “quite good” (43.2 versus 28%; p=0.002) and the ease of drinking the study preparation as “quite easy/very easy” (77.4 versus 56.8%; p<0.001). Significantly fewer adverse events were reported by patients taking MoviPrep versus NaP solution (7 versus 25%; p<0.0001). These studies both demonstrated that MoviPrep was comparable with regard to colon cleansing efficacy to older bowel preparations, but was preferred by more patients.

Halflytely plus Bisacodyl
Halflytely (Braintree Laboratories, Inc., Braintree) was the first 2L preparation introduced to the US market. The original formulation demonstrated colon cleansing efficacy comparable to that of 4L PEG, but with fewer adverse events.24 With the original formulation, patients took 20mg (four tablets) of bisacodyl followed within six hours by 2L of PEG. Recently, the amount of bisacodyl has been reduced from 20 to 10mg (two tablets). This new formulation is associated with fewer reports of nausea, abdominal cramming and fullness, vomiting and overall discomfort versus the original formulation with 20mg of bisacodyl.25

LoSo Prep™
LoSo Prep™ (E-Z-EM; Lake Success) contains low-sodium magnesium citrate and bisacodyl tablets and a suppository. Magnesium carbonate, citric acid and potassium citrate for oral solution are added to 8oz of water. The oral solution and 20mg (four tablets) of bisacodyl are taken the evening before.

On the morning of the procedure, patients insert a bisacodyl suppository. Magnesium citrate is a hyperosmotic saline laxative. It is eliminated by the kidneys and should not be used in patients with renal disease or impaired renal function. LoSo Prep contains less than 35g of sodium and patients need to take only 8oz of liquid, although additional fluid is usually recommended. The amount of magnesium citrate was recently increased by 10% from 34 to 37.9g. In a small pilot study with 17 patients, adequate colon cleansing was achieved by 85% of patients.26 All rated the taste of the preparation as tolerable or better. In a study comparing LoSo Prep with a standard 90ml dose of NaP solution taken throughout the day before colonoscopy, effective colon cleansing (score of excellent or good) was achieved by more than 80% of patients.27 Significantly more patients found the LoSo preparation tolerable (93 versus 83%; p<0.01) and were more likely to use the same preparation in the future (85 versus 71%; p<0.001) versus NaP solution. Although these studies report the safety and efficacy of LoSo Prep, larger, more well-controlled studies are necessary.

Conclusion
High-quality bowel preparation is critical for a successful colonoscopy. Bowel preparations need to be safe and work quickly without producing gastrointestinal distress. Several improvements have been made over the past few years to bowel preparations, including enhanced taste, reduction in volume and easier-to-use formulations. These improvements are likely to improve the quality of bowel preparation, adenoma detection rate, overall efficiency of colonoscopy and colon cancer screening rates.■